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USE OF VITAMIN E FOR DESENSITIZATION IN PREGNANCY COMPLICATIONS DUE TO Rh-INCOMPATIBILITY BETWEEN MOTHER AND FETUS

[Following is a translation of an article by F. M. Alizade, G. A. Guseynov, and G. S. Aleskerov in the Azerbaijani-language periodical Azerbaijan Tibb Zhurnali (Azerbaijan Medical Journal), Baku, No 2, February 1960, pages 28-32.]

In maternity hospitals habitual miscarriages, premature birth, stillbirth, hemolytic jaundice, generalized oedema, serious anemia, as well as congenital hemolytic diseases in abortive pregnancy, are frequently encountered.

However, the causes of these diseases have remained unclarified for a long time, as has the cause of post-transfusion reaction in connection with group-compatible blood transfusion. Advanced by Prof. V. N. Krainskaya-Ignatiyeva for the first time in 1934, the possibility of isosensitization and isoimmunization in the organisms of the fetus and the pregnant woman has become the basis of research on this problem.

Hereafter, the discovery of isoantigens (such as ABO, Rh-Hr, Kelle, Duffy, Le, Lu, etc.) which possess various systems in the blood, proved that isosensitization and isoimmunization take place in the organism of the mother when the blood of the fetus and mother are incompatible due to the mentioned isoantigens.

The isoimmune antibodies which appear later react with antigens of the fetus and hamper its normal development. For this reason, in the maternity practice special attention is given to isoantigen incompatibility between the blood of the fetus and the mother. A method in use is desensitizing the organism of isosensitized pregnant women in order to prevent overweight during pregnancy. Pharmacological and biological methods are used to desensitize isoimmunized pregnant women. The pharmacological method employs such means as cortisone, ACTH, adrenocorticotrophic hormone, progesterone, sodium salicylate, vitamins C, K, etc. The biological means used are haptens, antigens, whooping cough and typhus vaccines, and the human group antigens recently suggested by R. Papivanov.

The fundamental thesis of R. Papivanov is not acceptable. It asserts that the A and B group factors are comparatively stronger antigens than the Rh-Hr system factors. However, the immunization properties of the Rh-Hr system factors are actually stronger than the A and B group factors. Consequently the A and B group factors are not able to vie with the Rh factor, which is an active antigen in human blood.

The research conducted on this problem by F. M. Alizade (1956-1958) and T. G. Solovyov (1957) confirms all the above. T. M. Novchenko (1957) also came to the same conclusion. Moreover, the suggested thesis of R. Papivanov cannot be applied in the isosensitization of pregnant women who belong to the A and B group. His method is also not applicable in individual cases of contraindication regarding blood transfusions from other groups in such women by reason of their state of health.

In 1956, F. M. Alizade perfected an original method for the treatment of pathological pregnancy in connection with isoimmunization. With this method of treatment it is possible to prevent 95 percent of the cases of habitual miscarriage, stillbirth, and hemolytic anemia.

We have observed many contraindications pertaining to the matter of desensitization by vitamin E. Thus we studied the effect of vitamin E along with other desensitizing substances.

According to the studies of S. N. Astakhov (1954), R. L. Shub (1957), etc., on the normal development of the fetus, on the first day the fertilized egg is implanted it requires a sufficient quantity of vitamins A, B, C, and E, since vitamin insufficiency may cause the egg to perish. They determined that abortive pregnancy is very common among women suffering vitamin deficiency. Thus the incidence of premature births are 2.5 times, and stillbirths 4 times, greater among women suffering vitamin deficiency than in those who obtain a sufficient quantity of vitamins.

In order to prevent possible premature delivery, R. S. Mirsagatova, a research worker of the Kharkov Scientific Research Institute of the Ukrainian Academy of Medicine (UAM), applied vitamin E to induce desensitization in connection with isoantigen incompatibility between fetus and mother. But, according to the experimental observations of Prof. V. N. Krainskaya-Ignatiyeva, vitamin E is not practical for desensitizing the organism of a pregnant woman.

We observed the desensitization effect of vitamin E under experimental and clinical conditions. The experimental part of our work was carried out with the approval of the Minister of Health USSR (24 February 1956). We immunized 22 guinea pigs with Group O, Rh-positive human blood. As a result of this Rh-factor immunization Rh-antibodies were discovered in the serum of only seven of the 22 guinea pigs. It was impossible to detect Rh-antibodies in the serum of the remaining 15 guinea pigs. The titre of the immune Rh-antibodies in the serum of the immunized guinea pigs varied between 1:2 and 1:64.

In order to observe the desensitizing properties of vitamin E, a 30-50 mg dose of vitamin E was injected intramuscularly into each of the seven immunized pigs. During the period of desensitization each of the pigs had 10 vitamin E injections. In determining the titre of the immune Rh-antibodies in the serum of the guinea pigs, three separate control experiments were conducted: the first before the injections of vitamin E; the second after the tenth injection; and the third 10 days after the final injection.

From time to time, in order to obtain the in vitro titre of the Rh-antibodies, the capsulated serum of the guinea pigs, obtained before the vitamin E injections, was used.

The results of the research showed that the vitamin E injections did not decrease the titre of the immune Rh-antibodies in the serum of five of the immunized guinea pigs. The titre of the immune Rh-antibodies in the serum of the remaining two guinea pigs dropped to zero. This was not due to the vitamin E injections, but to the properties of the antibodies. The control experiment carried out to determine the titre of the immune Rh-antibodies (finished before the vitamin E application) also showed that the titre of the Rh-antibodies dropped to zero.

We also administered vitamin E to eight pregnant women who were isoimmunized against the Rh-factor. These pregnant women were of the same compatible blood group but were Rh-incompatible with their husbands. Before the vitamin E treatment, it was discovered that they had isoimmune Rh-antibodies in their serum with a titre between 1:2 and 1:32.

The anamnesis of the above-mentioned women revealed that they had an over-all incidence of one to 12 abortive pregnancies. These terminated in miscarriages, premature deliveries, stillbirths, and the delivery of infants with congenital hemolytic diseases. The Wassermann test was repeatedly administered to both the pregnant women and their husbands to make sure that there was no syphilis.

For the purpose of desensitization, the pregnant women were treated with vitamin E between the second and fourth month of pregnancy. Vitamin E was injected in an intramuscular dosage of 100-300 mg every 1-2 days, a total of 30-40 injections being given.

In order to obtain the titre of the isoimmune Rh-antibodies, three separate tests were made: one before the vitamin E injections; one after 20-25 injections of vitamin E; and one after an abortive pregnancy. Agglutination, conglutination, and results of the Coombs test were observed.

The results of our research are shown in the table below:

Names of the sensitized women	Titre of isoimmune Rh-antibodies			Month of pregnancy when treatment began
	Before application of vitamin E	After 20-25 injections	Results after abortive delivery	
V.T.	1:32	1:64	1:128	4
D.T.	1:16	1:16	1:64	3
G.L.	1:16	1:16	1:32	3
U.T.	1:16	1:32	1:32	3
T.A.	1:8	1:32	1:64	2.5
I.I.	1:8	1:8	1:8	3
I.R.	1:4	1:8	1:16	2
K.B.	1:2	1:4	1:8	3

As can be seen from the table, the titre of the isoimmune Rh-antibodies varied between 1:2 and 1:32 in the serum of the sensitized pregnant women before they were treated with vitamin E.

After 20-25 injections of vitamin E, it can be seen that the titre of the isoimmune Rh-antibodies in the serum did not fall, but, on the contrary, increased considerably. In the abortive deliveries, the results of the study of the titre of isoimmune Rh-antibodies revealed that vitamin E did not aid in decreasing the isoimmune Rh-antibodies. We observed increases in the titre of isoimmune Rh-antibodies in the serum in all the cases of abortive pregnancy.

Finally, of the eight women who were under observation, four delivered stillborn infants in the seventh to eighth months; two had miscarriages during the second half of pregnancy (fifth to sixth months); and the remaining two gave birth to infants with severe hemolytic jaundice, these infants dying 12 hours after birth.

Below is a brief history of two women who had abortive pregnancies.

1. The pregnant woman U.T. was born in 1923 and had been married since 1951. Her anamnesis reveals that she had three stillbirths, after the seventh to eighth month of pregnancy.

To protect her fourth pregnancy, the Women's Blood Transfusion Institute was consulted. A blood test showed that this woman belonged to the AB blood group, Rh-negative. She had isoimmune Rh-antibodies in her serum with a titre of 1:16. Her husband was Group A, Rh-positive.

Treatment was started in the third month of pregnancy with 300 mg of vitamin E injected intramuscularly every second day. She had a total of 40 injections.

Heart beat and movement ceased in the fetus in the seventh month of pregnancy. Fifteen days later she had a stillbirth. The titre of the isoimmune Rh-antibodies was 1:32 after this abortive pregnancy.

2. The pregnant woman D.T. was born in 1931. Her anamnesis shows that she was 4 times pregnant. Three of these pregnancies resulted in stillbirth in the seventh to eighth month of pregnancy. The fourth ended in miscarriage in the second half of pregnancy.

To protect her fifth pregnancy, the Women's Blood Transfusion Institute was consulted. Her blood test revealed her to be Group A, Rh-negative. She had isoimmune Rh-antibodies in her serum with a titre of 1:16. Her husband was Group O, Rh-positive.

Treatment was started in the third month of pregnancy with 300 mg of vitamin E injected intramuscularly every second day. She had a total of 40 injections. In spite of this, her fifth pregnancy ended in stillbirth after 6-1/2 months.

The titre of the isoimmune Rh-antibodies was 1:64 after this abortive delivery.

Conclusions

1. The titre of the immune and isoimmune Rh-antibodies in the serum did not decrease with the application of vitamin E in both the experimental conditions and the isoimmunization of the pregnant women.

2. It was impossible to prevent abortive pregnancy by giving vitamin E to the sensitized women who were under treatment.

3. Considering the desensitization ineffectiveness of vitamin E in pathopregnancy in connection with Rh-incompatibility between fetus and mother, we advise that vitamin E not be further administered in such cases.

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